6-9-04

AF
1617

GEI-078

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	:	M. Hul
M. LANQUETIN et al	:	
Serial No.: 09/646,763	:	Group: 1617
Filed: September 20, 2000	:	
For: TOPICAL HORMONAL...ACTION	:	

475 Park Avenue South
New York, N.Y. 10016
June 8, 2004

REPLY BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants are filing a reply brief in response to the Examiner's Answer of April 8, 2004 wherein the Examiner maintained the rejections of record.

The Examiner stated that the claims were obvious over the Saunal et al reference which is equivalent to U.S. Patent No. 6,010,716 and Maillo et al taken in view of Winters et al. The Examiner has alleged that Saunal et al teaches a transdermal topical formulation using a solvent and absorption promoting agent and an active comprising a steroid nomegestrol and a film forming agent and that it also teaches the solvent or solubilizing agent may be isopropanol or ethanol and that the film-forming agent can also be PVP VA. The Malillo et al reference allegedly teaches a gel formulation for topical use containing progesterone compounds including nomegestrol with 20 to 40% of ethanol and 1 to 4% of polyethylene glycol and water. The Examiner concedes that they do not

teach the amount of nomegestrol as 0.05 to 1% in a composition and that the references do not teach film forming agents as methacrylates and cellulose nor do they expressly teach a plasticizing agent such as Labrasol and they do not teach the ratio of water, ethanol, propylene glycol and Labrasol in the preferred solid system nor do they expressly teach a method of using a topical nomegestrol composition to treat progesterone deficiency in a host. Allegedly, Winters et al obviates these grounds of rejection. The claims were further rejected on the same prior art taken in view of the Merck patent.

With respect to Applicants' arguments concerning no motivation to combine the teachings, the Examiner has stated that the invention is drawn to a topical transdermal composition and the cited prior art as a whole teaches a composition of nomegestrol useful for transdermal delivery of the same. Applicants' arguments concerning the difference between transdermal dosage form and gel with systemic delivery were not convincing because given the broadest reasonable interpretation of Applicants' claim, the Examiner considers any composition that delivers active agents through the dermal layer is a transdermal composition. With respect to the Winters et al reference, the Examiner deems that the claimed excipients are taught as being useful for formulating topical compositions and that it would have been obvious to incorporate well known topical excipients into a nomegestrol containing composition as suggested by the primary references absent any showing to the contrary.

Applicants respectfully request the Board of Patent Appeals and Interferences to reverse the Examiner's rejection since the technical teaching of the Saunal et al reference does not teach that the composition contains 0.1 to 20% nomegestrol acetate. It merely teaches in line 28 of column 5 that "these medicinal active principles comprising estradiol (in various different active such as adrenocorticoids, thyroid hormones, hypoglycaemiant agents, progestative steroids) will be incorporated into the compositions of the invention in a proportion in particular from 0.1% to 20% of the weight of these compositions." It is well specified that each active principle will be introduced at individualized concentrations known in the state of the art but there is no example of a composition containing nomegestrol acetate to clarify this point. Moreover, the Saunal et al compositions must contain a physiologically non-aqueous solvent. On the contrary, the solubilizing agent in Applicants' preferred embodiment is selected from the group consisting of an aqueous solvent or a mixture of aqueous solvents as indicated in claims 6 to 8 and is well supported by line 14 of page 4 of the specification. In the preparation of compositions on pages 8 and 9, it also appears that nomegestrol acetate is dissolved in an aqueous solvent.

With respect to the Maillo et al reference, this concerns the use of progesterone derivatives having the general formula I but nomegestrol is a 17-hydroxy-6-methyl-19-nor-pregna-4,6-diene-3,20-dione and is disclaimed from this disclosure. Indeed, nomegestrol as well as nomegestrol acetate according the D1 formula, n=0, R_3=hydrogen

and R_1=methyl and R_2=hydrogen. Therefore, they are not included in the formula I because it is specified in claim 1 and line 24 of page 3 that "when n=0, R_3 is hydrogen only if both R_1 and R_2 are an alkyl of 1 to 6 carbon atoms." Thus, compositions containing compounds of formula I are totally different from the compositions according to the present invention. Nomegestrol acetate is just mentioned in the reference as "a potent orally active 19-nor progesterone-derived progestin." (line 1 of page 7) and uses as a reference product for oral administration without any specific formulation. Therefore, Applicants disagree with lines 7 to 9 of page 4 of the Examiner's Answer.

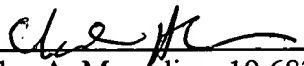
With respect to the Winters et al reference, this does not mention nomegestrol acetate in any fashion and teaches the use of a volatile solid in line 33 of page 3 through line 5 of page 4. Moreover; such a composition is destined to remain for a long contact with the skin. None of the references teach a composition containing nomegestrol acetate and an aqueous solubilizing agent for transdermal application. Moreover, the technical problems raised by each document are entirely different. In Saunal et al, the main problem is the flexibility of the matrix and the ability to remain for a long time in contact with the skin to get a sufficient rate. The Maillo et al reference describes nomegestrol acetate as a reference product for oral administration and in Winters et al, the main problem of the composition remains in the ability to be sprayable and the required use of a volatile solvent is taught.

None of these documents discloses how to achieve a topical composition which contains nomegestrol acetate and gives this active compound the ability to quickly cross the skin to induce systemic effects. Indeed, because of the specific properties of such a compound, it was thought to be impossible, particularly, nomegestrol as mentioned in the document Saunal et al among the long list of different and various compounds but the problems to solve for percutaneous application for such very different compounds are completely different. It is mentioned in line 10 of page 2 of Applicants' application that active principles penetrate through the skin depends on various physical, chemical, physiological parameters such as molecular characteristics, solubility, carriers and vehicles. On page 2 of the application, synthetic progestatives have specific lipophilic properties preventing them from crossing the skin and specific problems of percutaneous application of nomegestrol as well as nomegestrol acetate are solved by Applicants' invention using specific vehicles. Systemic effects and subject matter of the invention could not have been foreseen faced with these documents.

For this reason, Applicants disagree with the Examiner's statement on pages 8 and 9 and believe that there was absolutely no motivation to incorporate specific excipients into compositions suggested by the primary references and such a combination would not have provided Applicants' invention.

For these reasons, it is believed that the Examiner's reasoning in the Examiner's Answer are incorrect and Applicants request the Board of Patent Appeals and Interferences to respectfully traverse the Examiner's rejection. Three copies of this paper are being submitted.

Respectfully submitted,
Muserlian, Lucas and Mercanti



Charles A. Muserlian, 19,683
Attorney for Applicants
Tel.# (212) 661-8000

CAM:ds
Enclosures